P1 1105280

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APPLICATION NUMBER: *60/405,352*
FILING DATE: *August 23, 2002*
RELATED PCT APPLICATION NUMBER: *PCT/US03/26238*

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PTO/SB/16 (10-01)
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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
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Morteza	Naghavi	3525 Sage, Apt 1405, Houston, TX 77056

☐ *Additional inventors are being named on the _____ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

Methods and apparatus for non-invasively evaluating endothelial function

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

☐ Customer Number _____ → *Place Customer Number Bar Code Label here*

OR *Type Customer Number here*

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ENCLOSED APPLICATION PARTS *(check all that apply)*

☑ Specification *Number of Pages* 5
☑ Drawing(s) *Number of Sheets* 1
☐ Application Data Sheet. See 37 CFR 1.76
☐ CD(s), Number
☑ Other (specify) references

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

☐ Applicant claims small entity status. See 37 CFR 1.27.
☑ A check or money order is enclosed to cover the filing fees
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FILING FEE AMOUNT ($): $80.00

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☑ No
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Respectfully submitted,

SIGNATURE _____ Date 08/21/2002

TYPED or PRINTED NAME Morteza Naghavi

TELEPHONE _____

REGISTRATION NO. *(if appropriate)*
Docket Number:

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TOTAL AMOUNT OF PAYMENT ($) 80.00

Complete if Known	
Application Number	
Filing Date	08/21/2002
First Named Inventor	Morteza Naghavi, MD
Examiner Name	
Group Art Unit	
Attorney Docket No.	

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1. BASIC FILING FEE

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101	740	201	370	Utility filing fee	
106	330	206	165	Design filing fee	
107	510	207	255	Plant filing fee	
108	740	208	370	Reissue filing fee	
114	160	214	80	Provisional filing fee	

SUBTOTAL (1) ($) 80.00

2. EXTRA CLAIM FEES

	Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =		X =
Independent Claims		- 3** =		X =
Multiple Dependent				=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claim, if not paid
109	84	209	42	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

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FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	400	216	200	Extension for reply within second month	
117	920	217	460	Extension for reply within third month	
118	1,440	218	720	Extension for reply within fourth month	
128	1,960	228	960	Extension for reply within fifth month	
119	320	219	160	Notice of Appeal	
120	320	220	160	Filing a brief in support of an appeal	
121	280	221	140	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,280	241	640	Petition to revive - unintentional	
142	1,280	242	640	Utility issue fee (or reissue)	
143	460	243	230	Design issue fee	
144	620	244	310	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1.17(q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	740	246	370	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	740	249	370	For each additional invention to be examined (37 CFR § 1.129(b))	
179	740	279	370	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify) _____

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SUBMITTED BY				Complete (if applicable)	
Name (Print/Type)	Morteza Naghavi	Registration No. (Attorney/Agent)		Telephone	832-355-9144
Signature				Date	08/21/2002

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Title: - **Methods and apparatus for non-invasively evaluating endothelial function.**

Inventors: Nachiket Kharalkar
Dr. Morteza Naghavi

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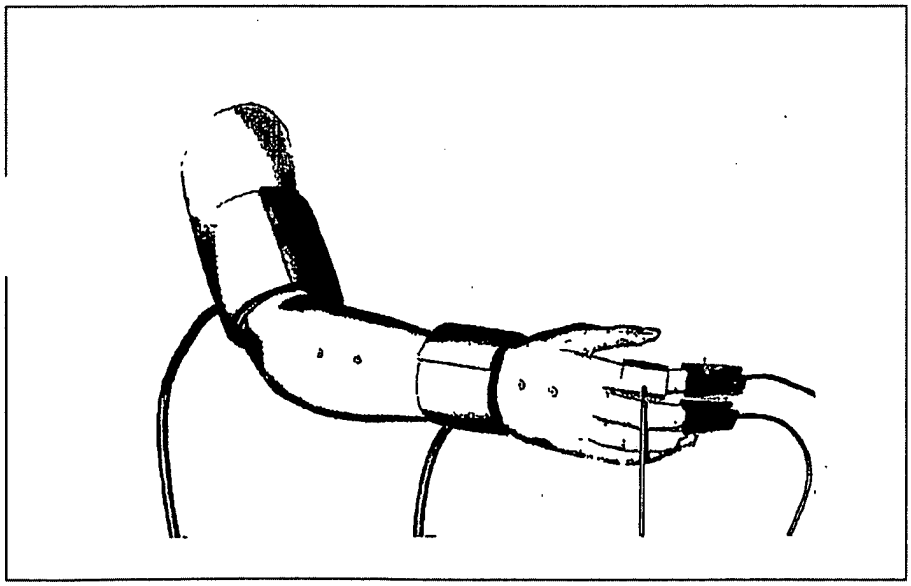
(List continued on next page.)

ABSTRACT

Methods and apparatus for non-invasively evaluating endothelial function. This can be done self-administratively without the presence of any medical practitioner. This test helps an ordinary consumer or patient to test the endothelial function and to obtain information about his endothelial cells; which are responsible for maintaining the patency and integrity of the arterial system. The hyperemia is simulated by creating an occlusion of the target artery (by inducing cuff pressure on arm, wrist, finger or leg) for some time and then suddenly releasing the occlusion. The changes in the arterial blood flow are monitored before the occlusion and then after the release of occlusion. Different techniques may be used to determine the blood flow through the arteries and may include but are not limited to pulse oximetry, temperature measurements, piezoelectric sensors or auditory sensors. These changes are then used to predict the endothelium dysfunction present if any.

restore to the application as [0030]



restore to the application as Figure 4

Methods and apparatus for non-invasively evaluating endothelial function

FIELD OF THE INVENTION

The present invention relates generally to evaluation of the endothelial function. More particularly, it allows medical examination of the vascular system, in the absence of the medical practitioner; at the public places such as shopping complex, airport, mall etc.

BACKGROUND OF THE INVENTION

Over the past two- three decades, the ability to diagnose heart disease has improved radically. This is primarily because of the evolution of new, increasingly sophisticated cardiac-testing techniques and equipments. Cardiovascular diseases and its sequel account for most of the morbidity and mortality in advanced countries. Although the exact cause of cardiovascular disease remains ambiguous, it is now know that an impairment of tissue perfusion represents the primary problem. The understanding of the development and progression of atherosclerosis has been greatly advanced in the past decade. In 1970's the response to injury hypothesis of atherosclerosis proposal was made; suggesting atherosclerosis begins with an injury to the arterial wall leading to endothelial denudation or 'stripping of the endothelial lining of the artery'. In recent years, it has become clear that the endothelium has many important functions in maintaining the patency and integrity of the arterial system. The endothelium can reduce and so inactivate toxic super-oxides which may be present in diabetics and in smokers. The endothelium is the source of the nitric oxide, a local hormone that relaxes the adjacent smooth muscle cells in the media, and is one of the most powerful vasodilators known. The endothelium regulates vascular homeostasis by elaborating a variety of paracrine factors that act locally in the blood vessel wall and lumen. Under normal conditions, the sum total effect of these endothelial factors is to maintain normal vascular tone, blood fluidity, and limit vascular inflammation and smooth muscle cell proliferation. However, when coronary risk factors are present, the endothelium may adopt a phenotype that facilitates inflammation, thrombosis, vasoconstriction, and atherosclerotic lesion formation. In human subjects, this maladaptive endothelial phenotype manifests itself prior to the development of frank atherosclerosis and is associated with traditional risk factors such as hypercholesterolemia, hypertension, and diabetes mellitus and with emerging risk factors such as hyperhomocystinemia, obesity, and systemic inflammation.

Possible causes of endothelial dysfunction include:-

- Elevated low density lipoprotein cholesterol, particularly oxidized LDL-C.
- Free radical induced damage caused by tobacco use, diabetes and hypertension.
- Genetic abnormalities.
- Elevated plasma homocysteine.
- Infectious agents such as Chlamydia.
- Obesity.
- Sedentary lifestyle.

Currently available methods for the estimation of the endothelial dysfunction can be classified in to two types; invasive and non-invasive methods.

Invasive methods are:-

1. Coronary endothelial function is frequently studied by measuring the vasodilator response of coronary arteries to acetylcholine or to cold pressor test by ~~invasive quantitative coronary angiography.~~ add to [0007]
2. Injecting the radioactive material, and then tracing the blood flow with the help of gamma ray radiations.

Non-invasive methods are:-

1. Method to evaluate the accuracy of measurement of the percent change in diameter of the left main trunk induced by cold pressor test with two-dimensional (2-D) echocardiography and extension of this method to the evaluation of coronary artery endothelial function in hypertensive patients.
2. Dundee step test.
3. Laser Doppler perfusion imaging and iontophoresis (Linton instruments).
4. High resolution B-mode ultrasound.
5. Detection of vascular conditions using an occlusive arm cuff plethysmograph.
6. Detection of medical conditions by monitoring the peripheral arterial tone, in conjunction with the creation of hyperemia by the arm cuff. add to [0008]

SUMMARY OF THE INVENTION

This Invention introduces a self administered endothelial function assessment test. The test is a non-invasive test for evaluation of endothelial function and can be done without the presence of any medical practitioner. The main endeavor for developing these tests is to enable an ordinary consumer or patient to test their endothelial function and get the information about his endothelial cells; which are responsible for maintaining the patency and integrity of the arterial system. In a self administered fashion this endothelial function assessment kit can be made available in the Check-my heart café, various public places, and also can be made home based.

This invention helps us in predicting the endothelial dysfunction non-invasively, without the presence of any medical practitioner. Currently available methods require the presence of skilled medical practitioner. These self administered endothelial function assessment tests can be performed at the public places and also at the home. The hospital based tests currently available are costly. The tests mentioned in this invention can be performed in 5-6 minutes. Currently available tests may sometimes require more than 6 minutes for the test.

restored as as paragraph [0012 - 13]

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is an overall system diagram of the invention, in its preferred embodiment.

restored as as paragraph [0018]

We claim:

1. A self administered method for non-invasive detection of the endothelial function of a person, without the intervention of any medical practitioner.

2. A method for self administered endothelial function evaluation comprising:
Creation of occlusion on the arm, leg, wrist or finger of a person in order to block the arterial blood flow;
Maintaining of the said occlusion for predetermined time at the predetermined pressure;
Removing the occlusion after predetermined period;
Monitoring of the changes in the oxygen content of the blood, temperature of finger tip or the blood flow rate;
Prediction of the EF from the analysis of above parameters.

restored as as paragraph [0031]

3. A method as mentioned in claim (2), wherein the pulse oximeter is connected to the tip of finger to continuously monitor the oxygen content of the blood in order to predict the EF.

restored as as paragraph [0032]

4. A method as mentioned in claim (2), wherein the temperature sensors are placed on the tip of the finger, to monitor the blood flow and predict the EF from that.

restored as as paragraph [0032]

5. A method as mentioned in claim (2), wherein two or more sensors separated by some known distance are placed on the forearm of the person when the occlusion is created in the arm, to determine the blood flow rate. The sensors may be pezio electric sensors, micro phone, pressure etc.

restored as as paragraph [0032]

6. A method as mentioned in claim (2), wherein Photoplethysmograph apparatus is placed near the finger to monitor the blood flow.

restored as as paragraph [0033]

7. A method as mentioned in claim (2), wherein two or more sensors separated by some distance are placed on the arm or the hand and the impedance between them is continuously monitored. This in turn gives the endothelial function.

restored as as paragraph [0033]

8. A method as mentioned in claim (2), wherein the blood flow is measured with the help of MAReNIR technique.

restored as as paragraph [0034]

9. A method as mentioned in claim (2), wherein the blood flow and the changes in the artery dimensions are monitored by the combined Ultrasound-Doppler technique.

restored as as paragraph [0034]

10. A method as mentioned in claim (2), which monitors the blood flow over the course of time right from before the creation of

restored as as paragraph [0035]

occlusion till the blood flow is normalized after the removal of the occlusion, in order to exactly predict the Endothelial function.

restored as as paragraph [0035]

11. A method as mentioned in claim (2), wherein the blood flow and the change in the blood flow are plotted against the time. These two graphs are further analyzed to give more accurate value of the endothelial function.

12. The self-administer endothelial function assessment system as mentioned in claim (1), which gives the 'Risk factor score' to the patient at the end of the test; indicating the amount of risk the user has.

restored as as paragraph [0035]

*****

[redacted]

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